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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,184	11/08/1999	JACK R. WANDS	04930/032001	6241

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
01/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/436,184	WANDS ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *10,14,39-50 and 72-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *10,14,39-50 and 72-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 9, 2007 has been entered.

Claims 10, 43, 72 and 74 have been amended. Claims 10, 14, 14, 39-50, 72-76 are pending and under consideration.

Claim 10 objected to because of the following informalities: the recited oligonucleotide is not properly labeled in accordance with the Sequence Rules. Amendment of the claim to recite "AAH sequence comprising nucleotides 1-11 of SEQ ID NO:3" would overcome this objection.. Appropriate correction is required.

The rejection of Claims 10, 13-15, 39-50, 72-76 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims have been amended to be dependent upon the coding sequence of SEQ ID NO:3, both of which are human sequences. Applicant has previously provided a declaration by Jack Wands averring that three different anti-sense constructs which fall under the scope of the amended claims reduced HAAH expression and inhibited tumor growth in vivo. This has been considered but not found persuasive. The instant claims are directed to the anti-sense modulation of the human AAH, and read on the inhibition of tumor growth in a human patient by the administration of a nucleic acid vector which transcribes a polynucleotide which is complementary of the HAAH regulatory coding sequence which is not disclosed. In the event that the claims were drawn to encompass a complementary coding region within SEQ ID NO:3,

the specification is not enabling for the claims requiring the inhibition of tumor growth in a mammal, which reads on the treatment of a human patient with a naturally occurring tumor for the following reasons.

Anti-sense therapy requires uptake of the administered polynucleotide by the target tumor cells. The specification does not provide dosage or data for administering a therapeutically effective dosage of the complementary sequences of the regulatory regions of SEQ ID NO:3, or SEQ ID NO:3 itself, to tumor cells which would result in the inhibition of growth, reproduction or survival of cancer cells. It is noted that many anti-sense therapies which appear to be promising using transfection in vitro, fail to provide any therapeutic efficacy when administered in vivo. Dar and Huang (Molecular Pharmaceutics, 2006, Vol. 3, pp. 2805-2809) teach that antisense therapy is hindered by poor stability in physiological fluids and limited intracellular uptake (abstract). In an article published eight years after the year of the instant filing, Sundaram et al (Nucleic Acids Research, 2007, Vol. 35, pp. 4396-4408) teach that despite the conceptual simplicity of the antisense approach, utilization of antisense is impaired by poor cellular entry and rapid degradation (page 579, second column, first full paragraph). Thus it can be concluded from these references that the art is unreliable with respect to in vivo treatment.

Because of all the deficiencies discussed above, and the unreliability in the art, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the claimed invention.

Applicant argues that the invention is based on the target molecule to which the therapy is directed, not to a delivery method per se. this has been considered but not found persuasive. the instant claims require the inhibition of tumor growth in a mammal and thus the delivery of an adequate dose of antisense compound is required.

Applicant argues that efficacy has been shown in an art recognized model of human cancer and it would be against patent law to require human clinical trial before the granting of a patent. this has been considered but not found persuasive. As stated above, the particular art of antisense therapy in patients is not mature. Major technical hurdles pertaining to stability of the administered nucleic acids in vivo and uptake of an adequate amount of the administered nucleic

acid still remain as problems seven years after the priority date of the instant application. The M.P.E.P. § 2164.05(b) states.

> The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification.

In the instant case, both the prior art and the post-filing date art support the notion that antisense therapy in a patient rather than and experimental model, although conceptually simple, is not a reliable treatment method.

All other rejections and objections as set forth in the prior action are withdrawn.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A. Canella/

Ph.D., Primary Examiner

Art Unit 1643